ANEMIA

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inflammatory or debilitating diseases like chronic infections, chronic liver disease, renal failure, hypothyroidism can cause anemia.

c) Bone marrow suppression or failure

Cytoxic drugs used to treat cancers can cause profound marrow suppression and thus decrease red cell formation also. Exposure to radiation, accidental or for treatment of cancer can suppress the marrow, thus leading to anemia.

Marrow failure due to conditions like aplastic anemia can present as anemia.

d) Marrow infiltration

In conditions like leukemia, lymphoma, myeloma and metastasis to the marrow, anemia is due to encroachment of marrow space by tumor thus suppressing normal erythropoiesis.

2. Anemia due to increased red cell destruction

This could be due to:

a) Congenital hemolytic anemias

Hemoglobinopathies: Congenital hereditary abnormalities of hemoglobin lead to formation of defective hemoglobin. Red cells containing defective hemoglobin are destroyed earlier in the reticuloendothelial system compared to red cells with normal hemoglobin, thus leading to ineffective erythropoiesis and hence anemia. eg: Thalassemias, sickle cell anemia.

Membranopathies: Congenital hereditary defect in red cell membrane which leads to early destruction of red cells by the reticuloendothelial system causing anemia. eg: hereditary spherocytosis, elliptocytosis.

Enzymopathies: Deficiency of certain enzymes present in the red cells eg: glucose-6-phosphate dehydrogenase leads to hemolysis of red cells on exposure to certain drugs or infections.

b) Acquired hemolytic anemia

Auto immune hemolytic anemia: secondary to conditions like SLE, Leukemia or even drug induced (quinine, methyl dopa etc). Hemolysis secondary to severe valvular heart disease and prosthetic valves.

3. Anemia due to blood loss

a) Trauma

b) Operative and post operative blood loss

c) Blood loss from the GI tract: esophageal varices, NSAID induced gastroduodenal lesions like peptic ulcer and erosions, arthritismenorrhagia, haemorrhoids, malignancy etc.

d) Menorrhagia, ante partum hemorrhage, post partum hemorrhage in women of child bearing age.

e) Frequent blood donation.

Blood loss anemia includes the entire clinical spectrum ranging from acute fulminant bleeding producing hypovolemic shock to chronic occult blood loss leading to iron deficiency anemia. Genito urinary tract is the most common site of blood loss in women of child bearing age while in men it is the GI tract.

Management of anemia depends on the identification of the cause of anemia and its reversal. Inappropriate use of hematinics such as iron in every patient of anemia for prolonged periods can be harmful, leading to iron overload. Similarly red cell transfusions are not the answer to every patient with anemia. Risks and complications of transfusion are many and well known. Hence it is important to know the etiology of anemia and treat it accordingly.

INTRODUCTION

Anemia whether clinically overt or not, is a common condition encountered in practice in our country. In view of this, it is important not only to look for clinical evidence of anemia but also investigate for the presence of anemia, even if the patient has definite evidence of other disease. This approach has another justification also; large number of non hematological disorders produce anemia. It is also important to remember this while dealing with patients with anemia, because at times anemia may be first and only evidence of some other underlying disease. Diagnostic label of ‘anemia’ should not be considered adequate, it is necessary to uncover the cause of anemia that would determine the treatment for anemia.

Approach to a patient of anemia begins with history taking, followed by clinical examination and then laboratory and other investigations.

HISTORY

Onset, duration and progress

Insidious onset, long duration and gradual progress of symptoms in a patient with anemia suggests nutritional anemia, chronic hemolytic anemia (congenital or acquired), anemia of chronic disease and anemia due to chronic blood loss. Rapid onset, short duration and rapid progress of symptoms indicate acute leukemia, acute hemolytic anemia, hemolytic/aplastic crisis in chronic hemolytic anemia, anemia secondary to acute blood loss, infiltrative disorders of the bone marrow.

Presence of symptoms other than those due to anemia is a pointer to underlying disease causing anemia and provide clue for further work up of the patient. Inquiry should be made to uncover conditions that may cause gastrointestinal, genitor-urinary or any other blood loss. Anemic patient who complains of angina or symptoms of cerebral hypoxia is in urgent need for raising his oxygen carrying capacity by red cell transfusions, whatever may be the cause of anemia.

Passage of high colored, dark red or brown urine indicates hemoglobinuria and intravascular hemolysis (auto immune hemolytic anemia, hemolysis in G-6-PD deficient individual, cold agglutinin disease, paroxysmal nocturnal hemoglobinuria, mismatched blood transfusion). History of episodes of bone pains, backache, abdominal pain in past suggests diagnosis of sickle cell disease.

Age & sex: Nutritional anemia is very common in our country and therefore it is encountered in both sexes and all ages although it is more common in pregnant women, females in reproductive age and children during phase of
to chronic blood loss and iron deficiency anemia. Certain drugs can cause hemolysis in individuals with G-6-PD deficiency. Rifampicin and alpha methyl dopa can cause autoimmune hemolytic anemia. Chemotherapeutic drugs can cause marrow depression and pancytopenia. Some drugs like chloramphenicol can cause marrow depression as an idiosyncratic reaction.

Family history of anemia, jaundice, gall stones or splenectomy should suggest possibility of hereditary hemolytic anemia. Community of the patient can be a pointer to diagnosis as thalassemias are more common amongst Sindhi and Lohana community, G-6-PD deficiency is more common amongst Bhanushalis and Parsees and sickle cell anemia is more common amongst tribal groups.

CLINICAL EXAMINATION

Clinical examination can provide a wealth of diagnostic information. A smooth pale (bald) tongue and nail changes (brittle, flat or concave nails; more common in toe nails than in finger nails), and bilateral painless parotid enlargement in a patient with anemia suggests the diagnosis of iron deficiency anemia. Skin pigmentation in peri-oral region and over knuckles is suggestive of megaloblastic anemia. Presence of jaundice would suggest possibility of hemolytic anemia. Generalized grayish discoloration of skin indicates iron overload in anemic patient who has been given transfusion over several years. Skin pigmentation and various skeletal abnormalities may be present in some cases of constitutional hypoplastic anemia. Presence of petechial hemorrhages would indicate

marrow infiltrative disease (leukemia, lymphoma, myeloma, metastasis, etc.); they may be seen in megaloblastic anemia also. Telangiectatic lesions on lips, tongue, conjunctiva, nasal mucosa, or finger tips should alert the clinician to possibility of recurrent GI bleeding as the cause of chronic debilitating anemia not responding to oral iron therapy. Presences of non healing ulcers on the legs suggest the possibility of sickle cell disease, hereditary spherocytosis or familial sideroblastic anemia.

Frontoparietal bossing, malar prominence, upper jaw and teeth projecting beyond the lower jaw, flat bridge of the nose – all giving rise to typical facial appearance are characteristic of thalassemia syndromes. Occasionally severe long standing iron deficiency anemia present since early childhood can give rise to similar facial appearance leading to wrong suspicion of thalassemia. Puffiness of lower eye lids, loss of eye brow hair and thick voice would reveal myxedema as the cause of anemia; this can be confirmed by delayed relaxation of muscle while eliciting deep reflexes.

Presence of hypertension should alert the clinician to possibility of anemia secondary to chronic renal failure.

Tenderness of calf muscles suggests megaloblastic anemia but could be present even in iron deficiency anemia. Signs of sub acute combined degeneration indicate pernicious anemia. Lymphadenopathy suggests possibility of leukemia or lymphoma. Minimal hepato-splenomegaly may be encountered in nutritional anemia but larger organomegaly should point to infiltrative disorder or parasitic diseases like malaria and kala azar.

INVESTIGATIONS

Complete blood count (including platelet count and reticulocyte count) with red cell indices (MCV, MCH and MCHC) and examination of peripheral blood smear are basic investigations which can provide morphological diagnosis and in some cases pathophysiological diagnosis. Hemoglobin of less than 14.0 g% in adult male, less than 12.0 g% in adult non-pregnant female, less than 11.0 g% in pregnant female and children should be considered as evidence of anemia. It is not uncommon for Indian clinicians to accept lower levels of Hb as normal (non-anemic) because large numbers of Indians have Hb in the range of 10-11 g% which is due to widespread nutritional iron deficiency in the country.

Hypochromic microcytic anemia (low MCV and low MCH) is commonly due to iron deficiency. Other cause of this type of anemia is thalassemia and anemia of chronic diseases. Presence of iron deficiency can be confirmed by estimating fetal hemoglobin and HbA2.

Macrocytic (high MCV) anemia indicates B12/ folate deficiency, hemolytic anemia with high reticulocyte count or even aplastic anemia.

Normocytic, normochromic (normal MCV and MCH) indicate anemia secondary to
chronic disease; investigations in this type of cases can be wide ranging depending on other findings and probable clinical diagnosis.

High reticulocyte count indicates active erythropoiesis in hemolytic anemia or in response to acute bleeding or response to hematonic therapy in deficiency anemia or infiltrative marrow disorder.

Peripheral smear examination can yield a wealth of information. Gross morphological abnormalities of red cells (hypochromia, microcytosis, anisocytosis, elliptocytosis, poikilocytosis, target cells, schistocytes) in a patient with Hb in range of 8-11 g% strongly suggests presence of beta thalassemia trait. Presence of microcytes indicates possibility of heditary spherocytosis, auto-immune hemolytic anemia or hemolytic disease of new born due to ABO incompatibility. Presence of schistocytes would indicate microangiopathic anemia. Leucoerythroblastic picture would indicate marrow infiltrative disorders (myeloma, metastasis, myelofibrosis, etc.). Presence of normoblasts in peripheral smear of patients with congestive cardiac failure signifies poor prognosis. Dimorphic anemia is best identified by peripheral smear examination showing microcytosis and macrocytosis, and hypochromia and normochromia. Presence of hypersegmented neutrophils (shift to right) indicates B12/folate deficiency.

In a hypochromic microcytic anemia, iron studies (serum iron, iron binding capacity, transferrin saturation; serum ferritin, marrow iron and plasma transferrin receptors) can clinch diagnosis of iron deficiency anemia. However, presence of coexisting B12/folate deficiency or chronic disease can interfere with diagnostic value of these investigations. Serum B12 and folate levels help identify deficiency of these hematinics.

Bone marrow examination helps in diagnosing megaloblastic anemia, iron deficiency, meyloedysplasia, hypoplastic and aplastic anemia, congenital dyserythropoietic anemia, sideroblastic anemia (congenital and acquired, primary and secondary, myelofibrosis, and marrow infiltrative disorders.

Stool examination for helminthiasis and occult blood can point to cause of iron deficiency anemia. Urine examination for proteins, pus cells, red cells, urobinogen and hemosiderin can provide explanation for anemia.

Endoscopies, barium studies, angiography and isotope studies would be needed to uncover source of blood loss from gastro-intestinal tract. However, these should be resorted to only when there is strong clinical suspicion of GI bleeding.

Hemoglobin electrophoresis, estimation of fetal hemoglobin, sickling test, Coombs test, test for cold agglutinins, osmotic red cell fragility, estimation of various red cell enzymes, etc would be needed in suspected case of hemolytic anemia.